

1  
SEQUENCE LISTING

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<120> HEPARANASE ACTIVITY NEUTRALIZING ANTI- HEPARANASE MONOCLONAL  
ANTIBODY AND OTHER ANTI-HEPARANASE ANTIBODIES

<130> 26128

<160> 11

<170> PatentIn version 3.2

<210> 1  
<211> 386  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<223> 45 kDa subunit of mature processed heparanase dimer

<400> 1

Lys Lys Phe Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu  
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Ala Leu Leu Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln  
35 40 45

Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu  
50 55 60

Leu Gly Asn Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile  
65 70 75 80

Asn Gly Ser Gln Leu Gly Glu Asp Phe Ile Gln Leu His Lys Leu Leu  
85 90 95

Arg Lys Ser Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly  
100 105 110

Gln Pro Arg Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala  
115 120 125

Gly Gly Glu Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn  
130 135 140

Gly Arg Thr Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp  
145 150 155 160

Ile Phe Ile Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr  
165 170 175

Arg Pro Gly Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly  
180 185 190

Gly Gly Ala Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp  
195 200 205

Leu Asp Lys Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met  
210 215 220

Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn  
225 230 235 240

Phe Asp Pro Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu  
245 250 255

Val Gly Thr Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg  
260 265 270

Lys Leu Arg Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr  
275 280 285

Lys Glu Gly Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr  
290 295 300

Lys Tyr Leu Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys  
305 310 315 320

Tyr Leu Leu Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val  
325 330 335

Gln Leu Asn Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro  
340 345 350

Pro Leu Met Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro  
355 360 365

Ala Phe Ser Tyr Ser Phe Phe Val Ile Arg Asn Ala Lys Val Ala Ala  
370 375 380

Cys Ile  
385

<210> 2  
<211> 535  
<212> PRT  
<213> Mus musculus

<400> 2

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Ala Gln Gly Ala Pro Ala Gly Thr Ala Pro Thr Asp Asp Val Val Asp  
20 25 30

Leu Glu Phe Tyr Thr Lys Arg Pro Leu Arg Ser Val Ser Pro Ser Phe  
35 40 45

Leu Ser Ile Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe Leu  
50 55 60

Thr Phe Leu Gly Ser Pro Arg Leu Arg Ala Leu Ala Arg Gly Leu Ser  
65 70 75 80

Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe  
 85 90 95  
 Asp Pro Asp Lys Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Lys Ser  
 100 105 110  
 Gln Val Asn His Asp Ile Cys Arg Ser Glu Pro Val Ser Ala Ala Val  
 115 120 125  
 Leu Arg Lys Leu Gln Val Glu Trp Pro Phe Gln Glu Leu Leu Leu Leu  
 130 135 140  
 Arg Glu Gln Tyr Gln Lys Glu Phe Lys Asn Ser Thr Tyr Ser Arg Ser  
 145 150 155 160  
 Ser Val Asp Met Leu Tyr Ser Phe Ala Lys Cys Ser Gly Leu Asp Leu  
 165 170 175  
 Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp Asn  
 180 185 190  
 Ser Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr  
 195 200 205  
 Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Trp Lys Lys  
 210 215 220  
 Ala His Ile Leu Ile Asp Gly Leu Gln Leu Gly Glu Asp Phe Val Glu  
 225 230 235 240  
 Leu His Lys Leu Leu Gln Arg Ser Ala Phe Gln Asn Ala Lys Leu Tyr  
 245 250 255  
 Gly Pro Asp Ile Gly Gln Pro Arg Gly Lys Thr Val Lys Leu Leu Arg  
 260 265 270  
 Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Leu Thr Trp His  
 275 280 285  
 His Tyr Tyr Leu Asn Gly Arg Ile Ala Thr Lys Glu Asp Phe Leu Ser  
 290 295 300  
 Ser Asp Ala Leu Asp Thr Phe Ile Leu Ser Val Gln Lys Ile Leu Lys  
 305 310 315 320  
 Val Thr Lys Glu Ile Thr Pro Gly Lys Lys Val Trp Leu Gly Glu Thr  
 325 330 335  
 Ser Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asn Thr Phe Ala  
 340 345 350  
 Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Gln Met Gly  
 355 360 365  
 Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His  
 370 375 380  
 Leu Val Asp Glu Asn Phe Glu Pro Leu Pro Asp Tyr Trp Leu Ser Leu  
 385 390 395 400

Leu Phe Lys Lys Leu Val Gly Pro Arg Val Leu Leu Ser Arg Val Lys  
 405 410 415  
 Gly Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn Val  
 420 425 430  
 Tyr His Pro Arg Tyr Gln Glu Gly Asp Leu Thr Leu Tyr Val Leu Asn  
 435 440 445  
 Leu His Asn Val Thr Lys His Leu Lys Val Pro Pro Pro Leu Phe Arg  
 450 455 460  
 Lys Pro Val Asp Thr Tyr Leu Leu Lys Pro Ser Gly Pro Asp Gly Leu  
 465 470 475 480  
 Leu Ser Lys Ser Val Gln Leu Asn Gly Gln Ile Leu Lys Met Val Asp  
 485 490 495  
 Glu Gln Thr Leu Pro Ala Leu Thr Glu Lys Pro Leu Pro Ala Gly Ser  
 500 505 510  
 Ala Leu Ser Leu Pro Ala Phe Ser Tyr Gly Phe Phe Val Ile Arg Asn  
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 Ala Lys Ile Ala Ala Cys Ile  
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 <213> Rattus norvegicus  
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 Asp Leu Glu Phe Tyr Thr Lys Arg Leu Phe Gln Ser Val Ser Pro Ser  
 35 40 45  
 Phe Leu Ser Ile Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe  
 50 55 60  
 Leu Thr Phe Leu Gly Ser Pro Arg Leu Arg Ala Leu Ala Arg Gly Leu  
 65 70 75 80  
 Ser Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile  
 85 90 95  
 Phe Asp Pro Asn Lys Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Gln  
 100 105 110  
 Ser Gln Asp Asn Asn Asp Ile Cys Gly Ser Glu Arg Val Ser Ala Asp  
 115 120 125  
 Val Leu Arg Lys Leu Gln Met Glu Trp Pro Phe Gln Glu Leu Leu Leu  
 130 135 140

Leu Arg Glu Gln Tyr Gln Arg Glu Phe Lys Asn Ser Thr Tyr Ser Arg  
 145 150 155 160  
 Ser Ser Val Asp Met Leu Tyr Ser Phe Ala Lys Cys Ser Arg Leu Asp  
 165 170 175  
 Leu Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp  
 180 185 190  
 Asn Ser Ser Asn Ala Gln Leu Leu Leu Asn Tyr Cys Ser Ser Lys Gly  
 195 200 205  
 Tyr Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Trp Lys  
 210 215 220  
 Lys Ala Gln Ile Ser Ile Asp Gly Leu Gln Leu Gly Glu Asp Phe Val  
 225 230 235 240  
 Glu Leu His Lys Leu Leu Gln Lys Ser Ala Phe Gln Asn Ala Lys Leu  
 245 250 255  
 Tyr Gly Pro Asp Ile Gly Gln Pro Arg Gly Lys Thr Val Lys Leu Leu  
 260 265 270  
 Arg Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Leu Thr Trp  
 275 280 285  
 His His Tyr Tyr Leu Asn Gly Arg Val Ala Thr Lys Glu Asp Phe Leu  
 290 295 300  
 Ser Ser Asp Val Leu Asp Thr Phe Ile Leu Ser Val Gln Lys Ile Leu  
 305 310 315 320  
 Lys Val Thr Lys Glu Met Thr Pro Gly Lys Lys Val Trp Leu Gly Glu  
 325 330 335  
 Thr Ser Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asn Thr Phe  
 340 345 350  
 Ala Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Gln Leu  
 355 360 365  
 Gly Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr  
 370 375 380  
 His Leu Val Asp Glu Asn Phe Glu Pro Leu Pro Asp Tyr Trp Leu Ser  
 385 390 395 400  
 Leu Leu Phe Lys Lys Leu Val Gly Pro Lys Val Leu Met Ser Arg Val  
 405 410 415  
 Lys Gly Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn  
 420 425 430  
 Val Tyr His Pro Arg Tyr Arg Glu Gly Asp Leu Thr Leu Tyr Val Leu  
 435 440 445  
 Asn Leu His Asn Val Thr Lys His Leu Lys Leu Pro Pro Pro Met Phe

450                      455                      460  
 Ser Arg Pro Val Asp Lys Tyr Leu Leu Lys Pro Phe Gly Ser Asp Gly  
 465                      470                      475                      480  
 Leu Leu Ser Lys Ser Val Gln Leu Asn Gly Gln Thr Leu Lys Met Val  
 485                      490                      495  
 Asp Glu Gln Thr Leu Pro Ala Leu Thr Glu Lys Pro Leu Pro Ala Gly  
 500                      505                      510  
 Ser Ser Leu Ser Val Pro Ala Phe Ser Tyr Gly Phe Phe Val Ile Arg  
 515                      520                      525  
 Asn Ala Lys Ile Ala Ala Cys Ile  
 530                      535  
 <210> 4  
 <211> 543  
 <212> PRT  
 <213> Homo sapiens  
 <400> 4  
 Met Leu Leu Arg Ser Lys Pro Ala Leu Pro Pro Pro Leu Met Leu Leu  
 1                      5                      10                      15  
 Leu Leu Gly Pro Leu Gly Pro Leu Ser Pro Gly Ala Leu Pro Arg Pro  
 20                      25                      30  
 Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro  
 35                      40                      45  
 Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn  
 50                      55                      60  
 Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu  
 65                      70                      75                      80  
 Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly  
 85                      90                      95  
 Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Ser Thr Phe  
 100                      105  
 Glu Glu Arg Ser Tyr Trp Gln Ser Gln Val Asn Gln Asp Ile Cys Lys  
 115                      120                      125  
 Tyr Gly Ser Ile Pro Pro Asp Val Glu Glu Lys Leu Arg Leu Glu Trp  
 130                      135                      140  
 Pro Tyr Gln Glu Gln Leu Leu Arg Glu His Tyr Gln Lys Lys Phe  
 145                      150                      155                      160  
 Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe  
 165                      170                      175  
 Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu  
 180                      185                      190  
 Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu

195	200	205
Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu Leu Gly Asn 210 215 220		
Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly Ser 225 230 235 240		
Gln Leu Gly Glu Asp Phe Ile Gln Leu His Lys Leu Leu Arg Lys Ser 245 250 255		
Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg 260 265 270		
Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu 275 280 285		
Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr 290 295 300		
Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe Ile 305 310 315 320		
Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr Arg Pro Gly 325 330 335		
Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly Gly Gly Ala 340 345 350		
Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp Lys 355 360 365		
Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met Arg Gln Val 370 375 380		
Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn Phe Asp Pro 385 390 395 400		
Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly Thr 405 410 415		
Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu Arg 420 425 430		
Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu Gly 435 440 445		
Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr Leu 450 455 460		
Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu Leu 465 470 475 480		
Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val Gln Leu Asn 485 490 495		
Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro Pro Leu Met 500 505 510		

Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro Ala Phe Ser  
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Tyr Ser Phe Phe Val Ile Arg Asn Ala Lys Val Ala Ala Cys Ile  
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<210> 5  
 <211> 523  
 <212> PRT  
 <213> Gallus gallus

<400> 5

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 1 5 10 15

Arg Thr Ala Glu Leu Gln Leu Gly Leu Arg Glu Pro Ile Gly Ala Val  
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Ser Pro Ala Phe Leu Ser Leu Thr Leu Asp Ala Ser Leu Ala Arg Asp  
 35 40 45

Pro Arg Phe Val Ala Leu Leu Arg His Pro Lys Leu His Thr Leu Ala  
 50 55 60

Ser Gly Leu Ser Pro Gly Phe Leu Arg Phe Gly Gly Thr Ser Thr Asp  
 65 70 75 80

Phe Leu Ile Phe Asn Pro Asn Lys Asp Ser Thr Trp Glu Glu Lys Val  
 85 90 95

Leu Ser Glu Phe Gln Ala Lys Asp Val Cys Glu Ala Trp Pro Ser Phe  
 100 105 110

Ala Val Val Pro Lys Leu Leu Leu Thr Gln Trp Pro Leu Gln Glu Lys  
 115 120 125

Leu Leu Leu Ala Glu His Ser Trp Lys Lys His Lys Asn Thr Thr Ile  
 130 135 140

Thr Arg Ser Thr Leu Asp Ile Leu His Thr Phe Ala Ser Ser Ser Gly  
 145 150 155 160

Phe Arg Leu Val Phe Gly Leu Asn Ala Leu Leu Arg Arg Ala Gly Leu  
 165 170 175

Gln Trp Asp Ser Ser Asn Ala Lys Gln Leu Leu Gly Tyr Cys Ala Gln  
 180 185 190

Arg Ser Tyr Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe  
 195 200 205

Arg Lys Lys Ser Gly Ile Cys Ile Asp Gly Phe Gln Leu Gly Arg Asp  
 210 215 220

Phe Val His Leu Arg Gln Leu Leu Ser Gln His Pro Leu Tyr Arg His  
 225 230 235 240

Ala Glu Leu Tyr Gly Leu Asp Val Gly Gln Pro Arg Lys His Thr Gln  
 245 250 255

His Leu Leu Arg Ser Phe Met Lys Ser Gly Gly Lys Ala Ile Asp Ser  
 260 265 270  
 Val Thr Trp His His Tyr Tyr Val Asn Gly Arg Ser Ala Thr Arg Glu  
 275 280 285  
 Asp Phe Leu Ser Pro Glu Val Leu Asp Ser Phe Ala Thr Ala Ile His  
 290 295 300  
 Asp Val Leu Gly Ile Val Glu Ala Thr Val Pro Gly Lys Lys Val Trp  
 305 310 315 320  
 Leu Gly Glu Thr Gly Ser Ala Tyr Gly Gly Gly Ala Pro Gln Leu Ser  
 325 330 335  
 Asn Thr Tyr Val Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ala  
 340 345 350  
 Ala Arg Arg Gly Ile Asp Val Val Met Arg Gln Val Ser Phe Gly Ala  
 355 360 365  
 Gly Ser Tyr His Leu Val Asp Ala Gly Phe Lys Pro Leu Pro Asp Tyr  
 370 375 380  
 Trp Leu Ser Leu Leu Tyr Lys Arg Leu Val Gly Thr Arg Val Leu Gln  
 385 390 395 400  
 Ala Ser Val Glu Gln Ala Asp Ala Arg Arg Pro Arg Val Tyr Leu His  
 405 410 415  
 Cys Thr Asn Pro Arg His Pro Lys Tyr Arg Glu Gly Asp Val Thr Leu  
 420 425 430  
 Phe Ala Leu Asn Leu Ser Asn Val Thr Gln Ser Leu Gln Leu Pro Lys  
 435 440 445  
 Gln Leu Trp Ser Lys Ser Val Asp Gln Tyr Leu Leu Leu Pro His Gly  
 450 455 460  
 Lys Asp Ser Ile Leu Ser Arg Glu Val Gln Leu Asn Gly Arg Leu Leu  
 465 470 475 480  
 Gln Met Val Asp Asp Glu Thr Leu Pro Ala Leu His Glu Met Ala Leu  
 485 490 495  
 Ala Pro Gly Ser Thr Leu Gly Leu Pro Ala Phe Ser Tyr Gly Phe Tyr  
 500 505 510  
 Val Ile Arg Asn Ala Lys Ala Ile Ala Cys Ile  
 515 520

&lt;210&gt; 6

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Artificial sequence

&lt;220&gt;

&lt;223&gt; Functional peptide epitope of heparanase

&lt;400&gt; 6

Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys

1 5 10

<210> 7  
 <211> 19  
 <212> PRT  
 <213> Artificial sequence

<220>  
 <223> Functional peptide epitope of heparanase  
 <400> 7

Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe  
 1 5 10 15

Asp Pro Lys

<210> 8  
 <211> 15  
 <212> PRT  
 <213> Artificial sequence

<220>  
 <223> Functional peptide epitope of heparanase  
 <400> 8

Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Leu Lys Lys Ala  
 1 5 10 15

<210> 9  
 <211> 15  
 <212> PRT  
 <213> Artificial sequence

<220>  
 <223> Functional peptide epitope of heparanase  
 <400> 9

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 1 5 10 15

<210> 10  
 <211> 14  
 <212> PRT  
 <213> Artificial sequence

<220>  
 <223> Functional peptide epitope of heparanase  
 <400> 10

Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr Ala Thr Arg  
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<210> 11  
 <211> 74  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> 8 kDa subunit of mature processed heparanase dimer  
 <400> 11

Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro Leu His Leu  
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11

Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn Leu Ala Thr  
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Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu Arg Thr Leu  
35 40 45

Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr  
50 55 60

Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu  
65 70